

## **REMARKS**

### **Status of the Claims**

Claims 1, 3 to 9, 21, 22 and 25 to 27 are pending as shown in the response filed October, 2006.

### **Rejections Withdrawn**

Applicants note with appreciation that the rejections under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph have been withdrawn. (Final Office Action, page 2).

### **35 U.S.C. §103**

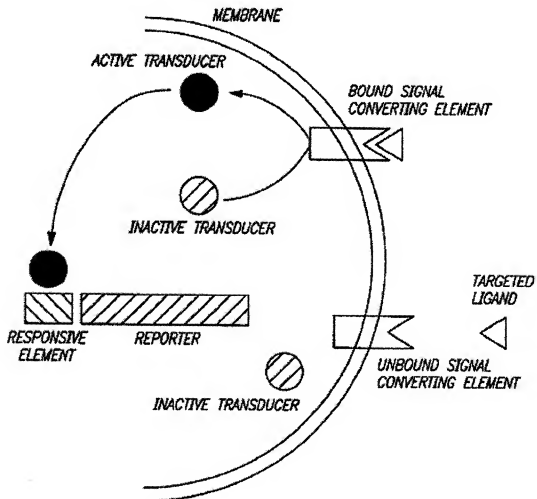
Claims 1, 3-9, 21, 22 and 27 were again rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,521,066 (hereinafter "Menzel") in view of U.S. Patent No. 5,348,867 (hereinafter "Georgiou"). (Final Office Action, pages 3-5).

Menzel was cited for disclosing a transmembrane fusion protein comprising a ligand binding domain, a cytoplasmic toxR NDA binding region, a hydrophobic ToxR transmembrane region and a reporter gene operably linked to the ctx operon. *Id.* Menzel was further alleged to disclose that binding a ligand to the ligand binding domain induces a conformational change in the cytoplasmic domain, which in turn induces binding to the promoter region of the reporter gene. *Id.* While the Office Action states that Menzel does not explicitly disclose use of antibodies on the bacterial surfaces, it was alleged that it would have been obvious to use Georgiou's heterologous scFV antibodies in Menzel's fusion proteins. *Id.*

It was also alleged that the fact that Menzel fails entirely to teach or suggest a transducer component as claimed (i.e. which is activated by the intracellular domain and in turn activates the responsive element) is not relevant because "the instant claims merely require a component that changes from an inactive to an active form in response to ligand binding and that that 'change' activates a responsive element resulting in a detectable signal." (Final Office Action, page 4, discussing Point 4).

In fact, the pending claims require that the component (transducer) that is changed from an inactive to an active form in response to ligand binding and then activates the responsive

element is separate from the intracellular domain. The claimed 3-component system (extracellular, intracellular and transducer) system is shown generally in FIG. 2 of the specification:



By contrast, Menzel's system completely lacks a transducer as claimed. Rather, the cytoplasmic (intracellular) domain of the Menzel's transmembrane protein acts directly on the promoter when the ligand is bound to the extracellular (ligand binding) domain (FIG. 1 of Menzel):

For the reasons of record, Georgiou fails to supply what is missing from Menzel. There is nothing whatsoever in this reference about transducers as claimed and, accordingly, no combination of Menzel and Georgiou that would result in the claimed 3-component biodetectors. On this basis alone, the rejection should be withdrawn.

For the reasons of record and as reiterated above, there is nothing in Menzel or Georgiou that would motivate the skilled artisan to (1) add a transducer that activates the responsive element to Menzel's systems and/or (2) combine such modified transducer-containing systems with Georgiou's scFvs. Not only do the references fail to teach all the limitations of the claims,

they fail to provide any motivation to make the modifications and combination suggested. Moreover, motivation to combine Menzel and Georgiou is not based on knowledge available at the time of filing, but on knowledge gleaned from Applicants' particular disclosure.

An obviousness rejection is only proper when it is based on common knowledge available at the time of filing. As clearly set forth in the recent Federal Circuit case *Dystar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 80 USPQ2d 1641 (Fed. Cir. 2006) (and every other case regarding obviousness), the motivation to combine cannot be based on what would be obvious after the specification at issue is filed. This is improper hindsight reconstruction (*Dystar* at page 1656):

As we recently explained in *Alza Corp. v. Mylan Labs., Inc.*, No. 06-1019, 2006 U.S. App. LEXIS 22616 [80 USPQ2d 1001] (Fed. Cir. Sept. 6, 2006), the suggestion test—as our motivation-to-combine inquiry has come to be known—“prevent[s] statutorily proscribed hindsight reasoning when determining the obviousness of an invention.”

Moreover, the common knowledge relied upon must be clearly set forth (*Dystar* at 1649, emphasis added):

Likewise, a close reading of *In re Lee* reveals that our objection was not to the Board's statement that “[t]he conclusion of obviousness may be made from common knowledge and common sense of a person of ordinary skill in the art without any specific hint or suggestion in a particular reference”, but **its utter failure to explain the “common knowledge and common sense” on which it relied.**

In the instant case, the Examiner has improperly based the obviousness rejection on a finding of what would be obvious in light of Applicants' disclosure, rather than what would have been obvious at the time of filing and has failed to set forth the “common knowledge” allegedly relied upon.

Indeed, the Examiner has not provided sound reasons supporting why the claims would have been obvious to the skilled artisan at the time of filing. The Office has not pointed to anything in the references or the common knowledge available at the time of filing that would motivate the skilled artisan to modify to include an activatable transducer and/or to combine

Menzel and Georgiou. As noted above in *Dystar*, a *prima facie* case of obviousness has not been made out because the Examiner's contention that the skilled artisan would have somehow had the knowledge to add a transducer as claimed to Menzel and then to combine these undisclosed transducer-containing systems with Georgiou's scFvs is completely unsupported by any reasoning "based on established scientific principles" that some advantage would have resulted from the hypothetical modifications.

It is only with Applicants' disclosure in hand that a skilled artisan would modify Menzel to include an activatable transducer molecule and/or combine Georgiou and with the modified systems of Menzel. See *In re Kotzab* 55 USPQ2d 1313, 1318 (Fed. Cir. 2000) and *Amgen, Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991) stating that "hindsight is not a justifiable basis on which to find that the ultimate achievement of a long sought and difficult scientific goal was obvious."

Accordingly, because there is no evidence that a skilled artisan would have made the suggested modifications and combination at the time of filing, the rejection is an impermissible hindsight reconstruction.

The alleged motivation to combine (increase specificity, diversity and ease of production) is not present in the references or in the common knowledge available at the time of filing. Without the benefit of Applicants' disclosure, a skilled artisan would have had no motivation to modify Menzel's systems to transducers as claimed. Accordingly, a *prima facie* case of obviousness has not been (and indeed cannot be) presented by the Office, as such a rejection can only be based on improper hindsight reconstruction. Withdrawal of the rejection is in order.

**CONCLUSION**

Applicants respectfully submit that the claims in condition for allowance.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Respectfully submitted,

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